## REMARKS

In the amendments presented herein, claims 1-3 and 5-10 have been cancelled without prejudice or disclaimer. Now pending in the application is claim 4. No new matter has been added.

The amendment and/or cancellation of claims is without prejudice or disclaimer of the subject matter thereof and was done solely to expedite prosecution of the present application. Applicants reserve the right to pursue the original subject matter of this application in a later filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject matter.

Applicants note with appreciation the Examiner's indication that certain prior objections to and rejections of the claims have been overcome. In view of the cancellation of claims 7 and 8, the rejection of these claims is moot and is not discussed further herein.

### Interview Summary

Applicants note with appreciation the Examiner's courtesy in permitting a telephonic interview with their undersigned representative on June 27, 2007. During the Interview, the pending claims and rejections of record were discussed; no final agreement was reached.

### Rejection under 35 U.S.C. §112, first paragraph (enablement)

Claim 4 stands rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. This rejection is traversed. Applicants offer the following remarks.

Claim 4 is directed to method of evaluating onset or onset possibility of rheumatoid arthritis in a human subject, the method comprising the step of: detecting the presence or absence of a gene coding a protein comprising the amino acid

sequence shown in SEQ. ID NO.:1 in the subject; and evaluating the onset or onset possibility of rheumatoid arthritis in the subject.

In Figure 4, the indicator "nt805(del3) homo" refers to the number of people having the normal gene homozygously, and the indicator "nt805(del3) hetero" refers to the number of people having the mutant gene heterozygously. In Figure 4, the indicator "nt805 homo" refers to the number of people having the mutant gene homozygously. In Figure 4, the label "Familial RA" refers to RA patients from RA families (69 subjects in Table 4), and the label "Sporadic RA" refers to RA patients from sporadic families (225 subjects). The label "Familial not RA" refers to healthy subjects from RA families (28 subjects), and the label "Sporadic not RA" refers to healthy subjects from sporadic families (383 subjects). Thus, the total number of RA patients is 294 (the sum of "Familial RA" and "Sporadic RA"), and the total number of healthy subjects (the total of "Familial not RA" and "Sporadic not RA") is 411.

As discussed previously and as shown in Figure 4, both in RA families and Sporadic families, only the RA patients have "nt805 homo" (homozygous 3-base-insertion mutation). The Examiner appears to agree that "it appears that an association exists for humans homozygous for the presence of 'GGT' at position 805-807" Office Action at page 5).

Furthermore, of the 294 RA patients, 223 (75.8%) are nt805(del3) homo, while 66 RA patients (22.4%) are nt805(del3) hetero. In contrast, of the 411 healthy patients, 373 (90.8%) are nt805(del3) homo, and only 38 (9.2%) are nt805(del3) hetero.

From the above, it can be said that the population of RA patients tend to have be "nt805(del3) hetero" (22.4%) more frequently than healthy patients are (9.2%). Therefore, Applicants urge that, in addition to evaluating the onset or onset possibility of RA by determining whether a subject is "nt805 homo," it is also possible to evaluate the onset or onset possibility of RA by determining whether a subject is "nt805(del3) hetero."

In the Wands analysis (under the heading "The state of prior art"), the Office Action states that certain references teach that "correlating gene expression level to any phenotypic quality" is unpredictable (Office Action at page 6). However, the Office

Action subsequently (at page 11) appears to withdraw this assertion. The Office Action states that "the instant invention is drawn to detection by quantitative PCR" (Office Action at page 11). Applicants point out that, as described in the specification and the previous Response, in certain embodiments, quantitative PCR can be used to measure the expression level of a gene; however, in other embodiments, other methods may be employed.

In the Wands analysis (under the heading "Quantity of experimentation necessary"), the Examiner states that "one would first have to determine if the claimed invention encompasses SEQ ID NO.1 with a glycine at positions 269 and 270, or a glycine at position 269, or no glycine at position 269 or 270." Office Action at page 7. Applicants disagree. As the Examiner indicated in the Office Action (at page 8) and in the Interview, claim 4 recites that the presence or absence of a gene coding a protein comprising the amino acid sequence shown in SEQ. ID NO.:1 is detected. Applicants submit that trial and error analysis as described by the Examiner would not be required to make and use the invention as claimed in claim 4.

The Examiner also states that "the skilled artisan would then have to determine if this insertion or deletion taught by the specification is by itself sufficient for diagnosing RA onset." Office Action at page 7. Applicants disagree. As noted above, in addition to evaluating the onset or onset possibility of RA by determining whether a subject is "nt805 homo," it is also possible to evaluate the onset or onset possibility of RA by determining whether a subject is "nt805(del3) hetero." Applicants submit that one of skill in the art would be able to practice the claimed method using no more than routine experimentation.

Applicants respectfully contend that the specification provides enablement for the full scope of the pending claim, and, furthermore, that the claim meets all the requirements of, *inter alia*, 35 USC §112. Reconsideration and withdrawal of the rejection is requested.

**CONCLUSION**

For at least the above reasons, Applicants contend that the application is in condition for allowance. Early and favorable consideration of the application is earnestly solicited.

While no extension of time is believed to be required, Applicants request any extension of time necessary for this response to be considered timely filed. The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Reference No. 61646 (70904), Customer No. 21874.

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Respectfully submitted,

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